IN THE CLAIMS

Please amend claim 1 as follows.

This listing of the claims replaces all prior versions of the claims in the application.

1. (Currently Amended) An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-2, and

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical [[to]] over the complete sequence of an amino acid sequence selected from the group consisting of SEQ ID NO:1-2, and which retains ubiquitin-conjugating activity.

~~c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-2, and~~

~~d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-2~~.

2. (Previously Amended) An isolated polypeptide of claim 1 selected from the group consisting of SEQ ID NO:1-2.

9. (Withdrawn) A method of producing a polypeptide of claim 1, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and

b) recovering the polypeptide so expressed.

10. (Withdrawn) An isolated antibody which specifically binds to a polypeptide of claim 1.

11. (Withdrawn) An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:4-6,

b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:4-6,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).

13. (Withdrawn) A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

14. (Withdrawn) A method of claim 13, wherein the probe comprises at least 60 contiguous nucleotides.

15. (Withdrawn) A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

16. (Original) A composition comprising a polypeptide of claim 1 and a pharmaceutically acceptable excipient.

17. (Previously Amended) A composition of claim 16, wherein the polypeptide has an amino acid sequence selected from the group consisting of SEQ ID NO:1-2.

18. (Withdrawn) A method for treating a disease or condition associated with decreased expression of functional UCEH, comprising administering to a patient in need of such treatment the composition of claim 16.

19. (Withdrawn) A method of screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:

a) exposing a sample comprising a polypeptide of claim 1 to a compound, and

b) detecting agonist activity in the sample.

20. (Withdrawn) A composition comprising an agonist compound identified by a method of claim 19 and a pharmaceutically acceptable excipient.

21. (Withdrawn) A method for treating a disease or condition associated with decreased expression of functional UCEH, comprising administering to a patient in need of such treatment a composition of claim 20.

22. (Withdrawn) A method of screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:

a) exposing a sample comprising a polypeptide of claim 1 to a compound, and

b) detecting antagonist activity in the sample.

23. (Withdrawn) A composition comprising an antagonist compound identified by a method of claim 22 and a pharmaceutically acceptable excipient.

24. (Withdrawn) A method for treating a disease or condition associated with overexpression of functional UCEH, comprising administering to a patient in need of such treatment a composition of claim 23.

25. (Withdrawn) A method of screening for a compound that specifically binds to the polypeptide of claim 1, the method comprising:

a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

26. (Withdrawn) A method of screening for a compound that modulates the activity of the polypeptide of claim 1, the method comprising:

a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,

b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

27. (Withdrawn) A method of screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

b) detecting altered expression of the target polynucleotide, and

c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

28. (Withdrawn) A method of assessing toxicity of a test compound, the method comprising:

a) treating a biological sample containing nucleic acids with the test compound,

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim
11 or fragment thereof,

c) quantifying the amount of hybridization complex, and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

45. (Original) A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:1.

46. (Original) A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:2.

REMARKS

The claims have been amended to clarify the invention.. In particular, claim 1 has been amended to delete "fragment language" in claim elements 2(c) and 2(d). Claim 1 has been further amended at 2(b) to recite a naturally occurring variant at least 90% identical "over the complete sequence of an amino acid sequence selected from... and which retains ubiquitin-conjugating activity". Support for the amendment to claim 1 is found in the specification, for example, at page 48, lines 25-31, which describes an assay for measuring ubiquitin-conjugating activity in the claimed polypeptides. No new matter is added by any of these amendments, and entry of the amendments is respectfully requested.

The Examiner stated that claims 1, 2, 16, 17, 45 and 46 are currently under examination. Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 1 and 16

The Examiner has rejected claims 1 and 16 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner stated that the claims are drawn to polypeptides comprising (a) the amino acid sequence of any one of SEQ ID NO:1-2, (b) an amino acid sequence having at least 90% identity to SEQ ID NO:1-2, (c) a biologically active fragment or immunogenic fragment of SEQ ID NO:1-2. The specification, however, teaches only 3 distinct proteins having the amino acid sequences of SEQ ID NO:1-3. The specification does not disclose and fully characterize any variants of these proteins which have the same or a different biological activity. No protein are exemplified which have 90%, 91%, etc identity with SEQ ID NO:1-2. Furthermore, the Examiner stated, the claims include biologically active fragments of SEQ ID NO:1-2, and the claims do not define the biological activity of the polypeptide and thereby encompass poypeptides having any biological activity. While the skilled artisan may identify fragments of SEQ ID NO:1-2, the specification does not teach fragments which have particular biological activities, e.g., ubiquitin activity. It is further noted that while the claims provide structural limitations for the encoded proteins, the claims do not define the functional properties of the encoded polypeptides.

The Examiner cited *Vas-Cath V. Mahurkar* and *The Regents of the University of California v. Eli Lilly* and the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" with respect to the requirements for adequate written description under this section.

Applicants Response

Claim 1 has been amended to delete fragment language. In addition, claim element 2(b) has been amended to recite the additional limitation that a naturally occurring variant having at least 90% identity over the complete sequence of SEQ ID NO:1 or SEQ ID NO:2 further retain the ubiquitin conjugating activity of SEQ ID NO:1 or SEQ ID NO:2. The specification describes an assay to measure ubiquitin conjugating activity at page 48, lines 25-31, and further describes a ubiquitin conjugating enzyme active site for SEQ ID NO:2 in the specification at page 15, lines 27-28. The skilled artisan would therefore readily recognize applicants possession of any such naturally occurring variants of SEQ ID NO:1 or SEQ ID NO:2 possessing ubiquitin conjugating activity. Furthermore, the Examination Guidelines which the Examiner refers to specifically states:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., **complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics**. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met (emphasis added).

Applicants submit that, based on the above requirements, the extensive chemical and structural characterization of ubiquitin conjugating proteins exemplified by SEQ ID NO:1 and 2 at pages 14-16 of the specification is adequate to meet this requirement. However, the additional functional limitation of a ubiquitin conjugating enzyme activity in the claims clearly meets the requirements under 35 U.S.C. § 112, first paragraph. Withdrawal of the rejection of claims 1-16 under 35 U.S.C. § 112, first paragraph is therefore requested.

35 U.S.C. § 102(b), Rejection of Claims 1 and 16

The Examiner has rejected claims 1 and 16 under 35 U.S.C. § 102(b) as anticipated by Korngold. Korngold teaches a peptide which consists of 6 amino acids identical to amino acids 216-221 of SEQ ID NO:1. The peptide of Korngold is considered to meet the limitations of claim 1 and 16 of an immunogenic and biologically active fragment of a polypeptide of SEQ ID NO:1.

The Examiner also stated that claim 1 is rejected under 35 U.S.C. § 102(b) as anticipated by Sun (BBA, March 1997). Sun et al teaches a ubiquitin conjugating protein which is identical to amino acids 1-234 of SEQ ID NO:2. It is noted that the claims as written include biologically active and immunological fragments of SEQ ID NO:2 and polypeptides having 90% identity over any length of SEQ ID NO:2. Thereby the protein of Sun meets the limitations of the claim.

Applicants Response

Claim 1 has been amended to delete fragment language and to recite a polypeptide having at least 90% identical over the complete sequence of SEQ ID NO:1 or SEQ ID NO:2. Neither Korngold or Sun anticipate a polypeptide having the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2, or a polypeptide having at least 90% identity over the complete sequence of SEQ ID NO:1 or SEQ ID NO:2. Withdrawal of the rejection of claims 1 and 16 as anticipated by either Korngold or SUN is therefore requested.

35 U.S.C. § 103(a), Rejection of Claims 1 and 16

The Examiner has rejected claim 1 and 16 under 35 U.S.C. § 103(a) as being unpatentable over Hillier et al (GenBank Accession No. AA195176) in view of Draetta (U.S. Patent No. 5,744,343). Hillier teaches isolated nucleic acids which encode for a human ubiquitin-conjugating enzyme. The nucleic acids of Hillier share 98% identity with the instant SEQ ID NO:4 (encoding SEQ ID NO:1). The Examiner further noted that the protein encoded by the nucleic acid of Hillier shares 100% identity with amino acids 33-181 of the present SEQ ID NO:1.

Hillier does not specifically teach the protein encoded by this nucleic acid or compositions comprising the protein and a pharmaceutically acceptable excipient. However, the Examiner stated, Draetta teaches cloning the nucleic acid encoding ubiquitin-conjugating enzymes into expression vectors, transforming cells with the vectors, and expressing the polypeptides. In view of Draetta, it would have been obvious to one of ordinary skill in the art to

have cloned the nucleic acids of Hillier into expression vectors, transform cells, and express the proteins, thus meeting the limitations of claim 1. Further, the Examiner stated, with respect to claim 16, Draetta teaches compositions comprising ubiquitin-conjugating enzymes and pharmaceutical carriers. Accordingly, it would have been obvious to one of ordinary skill in the art to provide a composition comprising the protein encoded by the Hillier nucleic acid useful for storage and administration, thus meeting the limitations of claim 16.

The Examiner stated further that claims 1 and 16 are unpatentable over Sun in view of Draetta. The teachings of Sun have been discussed previously. As previously noted, the claims include biologically active and immunogenic fragments of SEQ ID NO:2 and polypeptides having 90% identity over any length of SEQ ID NO:2, thereby meeting the limitations of the claims. Sun does not specifically teach a composition comprising the protein and a pharmaceutical carrier. It would have been obvious, however that in view of the teachings of Draetta previously stated, to combine the teachings of Sun and Draetta thus meeting the limitations of claim 16.

Applicants Response

The amendments to claim 1 have been discussed previously. Applicants submit that in order to establish a *prima facie* case of obviousness against a claim, the reference, or combination of references, must teach or suggest all of the claim limitations. Neither Hillier, Sun, or Draetta teach or suggest SEQ ID NO:1 or SEQ ID NO:2, or a polypeptide having 90% identity over the complete sequence of SEQ ID NO:1 or SEQ ID NO:2. There is therefore no proper *prima facie* case of obviousness against claims 1 or 16, and withdrawal of the rejection of claims under 35 U.S.C. § 103(a) is therefore requested.

Objection to Claims 2, 17, 45 and 46

The Examiner has objected to claims 2, 17, 45 and 46 as being dependent on a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicants Response

Applicants submit that having obviated all outstanding rejections to the rejected base claim (claim 1) and intervening claims (claim 16), that claims 2, 17, 45 and 46 are allowable as recited and withdrawal of the objection is therefore requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited. Applicants further request that upon allowance of claim 1, claims 9, 19, 22, 25, and 26 be rejoined and examined as methods of use of the polypeptides of claim 1 that depend from and are of the same scope as claim 1 in accordance with *In re Ochiai* and the MPEP § 821.04.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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